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NEWS 26 JUN 26 MARPAT Enhancements Save Time and Increase Usability  
NEWS 27 JUL 25 STN adds Australian patent full-text database,  
AUPATFULL, including the new numeric search feature.  
NEWS 28 AUG 01 CA Sections Added to ACS Publications Web Editions  
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USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2011

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=> s loline  
133 LOLINE  
33 LOLINES  
L1 140 LOLINE

(LOLINE OR LOLINES)

=> s 11 and bacteria  
421341 BACTERIA  
191 BACTERIAS  
421442 BACTERIA  
(BACTERIA OR BACTERIAS)

L2 1 L1 AND BACTERIA

=> d 12 ibib ab

L2 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2011 ACS on STN  
ACCESSION NUMBER: 2011:770722 CAPLUS  
TITLE: An efficient synthesis of loline alkaloids  
AUTHOR(S): Cakmak, Mesut; Mayer, Peter; Trauner, Dirk  
CORPORATE SOURCE: Department of Chemistry and Pharmacology and Center  
for Integrated Protein Science,  
Ludwig-Maximilians-Universitaet, Munich, 81377,  
Germany

SOURCE: Nature Chemistry (2011), 3(7), 543-545  
CODEN: NCAHBB; ISSN: 1755-4330

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB Loline (1) is a small alkaloid that, in spite of its simple-looking structure, has posed surprising challenges to synthetic chemists. It has been known for more than a century and has been the subject of extensive biol. investigations, but only two total syntheses have been achieved to date. Here, we report an asym. total synthesis of loline that, with less than ten steps, is remarkably short. Our synthesis incorporates a Sharpless epoxidn., a Grubbs olefin metathesis and an unprecedented transannular aminobromination, which converts an eight-membered cyclic carbamate into a bromopyrrolizidine. The synthesis is marked by a high degree of chemo- and stereoselectivity and gives access to several members of the loline alkaloid family. It delivers sufficient material to support a program aimed at studying the complex interactions between plants, fungi, insects and bacteria brokered by loline alkaloids.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s 11 and (antiinfective or antibacterial)  
1920 ANTIINFECTIVE  
145 ANTIINFECTIVES  
2017 ANTIINFECTIVE  
(ANTIINFECTIVE OR ANTIINFECTIVES)  
145234 ANTIBACTERIAL  
4350 ANTIBACTERIALS  
146518 ANTIBACTERIAL  
(ANTIBACTERIAL OR ANTIBACTERIALS)

L3 2 L1 AND (ANTIINFECTIVE OR ANTIBACTERIAL)

=> d 13 1-2 ibib ab

L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2011 ACS on STN  
ACCESSION NUMBER: 2008:918265 CAPLUS  
DOCUMENT NUMBER: 149:439128  
TITLE: Endophytes: exploiting biodiversity for the  
improvement of natural product-based drug discovery  
AUTHOR(S): Staniek, Agata; Woerdenbag, Herman J.; Kayser, Oliver  
CORPORATE SOURCE: Pharmaceutical Biology Department, University of

SOURCE: Groningen, Neth.  
 Journal of Plant Interactions (2008), 3(2), 75-93  
 CODEN: JPIOAG; ISSN: 1742-9145  
 PUBLISHER: Taylor & Francis Ltd.  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: English  
 AB A review. Endophytes, microorganisms that colonize internal tissues of all plant species, create a huge biodiversity with yet unknown novel natural products, presumed to push forward the frontiers of drug discovery. Next to the clin. acknowledged antineoplastic agent, paclitaxel, endophyte research has yielded potential drug lead compds. with antibacterial, antiviral, antioxidant, insulin mimetic, anti-neurodegenerative and immunosuppressant properties. Furthermore, while being implicated in livestock neurotoxicosis, some endophyte-produced alkaloids have been shown to display insecticidal activity. The endophyte-host relationship is postulated to be a 'balanced antagonism'. Moreover, the plausibility of horizontal gene transfer (HGT) hypothesis is taken into account. Knowledge of the genetic background of endophytic natural product biosynthesis is discussed on the basis of loline alkaloids, ergopeptides, lolitrems and maytansinoids. The current dynamic progress in genomics will contribute to a better understanding of endophytic microbes and to further exploiting them as a source of pharmaceutically relevant compds.  
 OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)  
 REFERENCE COUNT: 170 THERE ARE 170 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2005:451185 CAPLUS  
 DOCUMENT NUMBER: 142:487686  
 TITLE: Antibacterial compositions comprising (alkyl)aminopyrrolizidine compounds  
 INVENTOR(S): Nash, Robert James; Wolferstan, Paul; Fleet, George William John; Van Ameijde, Jeroen; Horne, Graeme  
 PATENT ASSIGNEE(S): Molecularnature Limited, UK; M N L Pharma Limited  
 SOURCE: PCT Int. Appl., 24 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005046674	A2	20050526	WO 2004-GB4624	20041103
WO 2005046674	A3	20050714		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: GB 2003-25655 A 20031104  
 OTHER SOURCE(S): MARPAT 142:487686

AB Antibacterial (alkyl)aminopyrrolizidine compds. for use in therapy or prophylaxis may be pharmaceutically acceptable derivs. of loline. Examples include 2,7-dihydroxy-1-methylaminopyrrolizidine, 2,7-dihydroxy-1-aminopyrrolizidine, 2-hydroxy-1-aminopyrrolizidine, 2-hydroxy-1-methylaminopyrrolizidine, 7-hydroxy-1-aminopyrrolizidine, 7-hydroxy-1-methylaminopyrrolizidine, 1 $\alpha$ -methylamino-2 $\beta$ -hydroxypyrrolizidine, 1 $\alpha$ -methylamino-7 $\beta$ -hydroxypyrrolizidine, 1 $\alpha$ -amino-2 $\beta$ -hydroxypyrrolizidine, 1 $\alpha$ -amino-7 $\beta$ -hydroxypyrrolizidine, 1 $\alpha$ -amino-2,7 $\beta$ -hydroxypyrrolizidine and 1 $\alpha$ -methylamino-2,7 $\beta$ -hydroxypyrrolizidine. The compds. may be used to treat infection with *Staphylococcus aureus* (MRSA), including C-MRSA1, C-MRSA2, C-MRSA3, C-MRSA4, Belgian MRSA, Swiss MRSA and any of the EMRSA strains. For example, meadow brown butterflies have activity against *Staphylococcus aureus* (MRSA) and a 50% ethanol extract of these butterflies contains the activity. Furthermore, the activity was retained by a strongly acidic cation exchange resin. The material not bound to the resin was inactive but the material displaced by 2 M ammonia solution had activity. This ammonia fraction contained various open-furan ring lolines (as determined by mass spectroscopy). Also, a semisynthetic reaction mixture derived from loline was tested for activity by incubation for 12 to 24 h at 37° at various concns. with a suspension of 1x10<sup>3</sup> c.f.u. of *Staphylococcus aureus*. After incubation, test samples were plated onto solid agar plates and colonies counted after incubation at 37° for 24 h. Complete bacterial killing was observed

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s aminopyrrolizidine  
 10 AMINOPYRROLIZIDINE  
 9 AMINOPYRROLIZIDINES  
 L4 17 AMINOPYRROLIZIDINE  
 (AMINOPYRROLIZIDINE OR AMINOPYRROLIZIDINES)

=> d l4 1-17 ibib ab

L4 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2009:905355 CAPLUS

DOCUMENT NUMBER: 151:381149

TITLE: Synthesis of polyhydroxylated 7-aminopyrrolizidines and 8-aminoindolizidines

AUTHOR(S): Stecko, Sebastian; Jurczak, Margarita; Staszewska-Krajewska, Olga; Solecka, Jolanta; Chmielewski, Marek

CORPORATE SOURCE: Institute of Organic Chemistry, Polish Academy of Sciences, Warsaw, 01-224, Pol.

SOURCE: Tetrahedron (2009), 65(34), 7056-7063

CODEN: TETRAB; ISSN: 0040-4020

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 151:381149

AB The ammonolysis of a lactone moiety in tricyclic cycloadducts derived from non-racemic five-membered cyclic nitron and 2(5H)-furanones furnishes an amido function, which after subsequent Hofmann rearrangement, leads to a protected amino group attached to the bicyclic isoxazolidine skeleton. A successive simple transformation, involving cleavage of N-O bond followed

by intramol. N-alkylation, provides an access to the polyhydroxylated 7-aminopyrrolizidines and 8-aminoindolizidines, i.e. I, potential glycosidases inhibitors.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)  
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2008:1065320 CAPLUS

DOCUMENT NUMBER: 151:96719

TITLE: Role of the LolP cytochrome P450 monooxygenase in loline alkaloid biosynthesis

AUTHOR(S): Spiering, Martin J.; Faulkner, Jerome R.; Zhang, Dong-Xiu; Machado, Caroline; Grossman, Robert B.; Schardl, Christopher L.

CORPORATE SOURCE: Department of Plant Pathology, University of Kentucky, Lexington, KY, 40546-0312, USA

SOURCE: Fungal Genetics and Biology (2008), 45(9), 1307-1314  
CODEN: FGBIFV; ISSN: 1087-1845

PUBLISHER: Elsevier Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The insecticidal loline alkaloids, produced by *Neotyphodium uncinatum* and related endophytes, are *exo*-1-aminopyrrolizidines with an ether bridge between C-2 and C-7. Loline alkaloids vary in Me, acetyl, and formyl substituents on the 1-amine, which affect their biol. activity. Enzymes for key loline biosynthesis steps are probably encoded by genes in the LOL cluster, which is duplicated in *N. uncinatum*, except for a large deletion in lolP2. The role of lolP1 was investigated by its replacement with a hygromycin B phosphotransferase gene. Compared to wild type *N. uncinatum* and an ectopic transformant, A1olP1 cultures had greatly elevated levels of N-methyllooline (NML) and lacked N-formyllooline (NFL). Complementation of A1olP1 with lolP1 under control of the *Emericella nidulans* trpC promoter restored NFL production. These results and the inferred sequence of LolP1 indicate that it is a cytochrome P 450, catalyzing oxygenation of an N-Me group in NML to the N-formyl group in NFL.

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2007:539557 CAPLUS

TITLE: Intermediate steps of loline alkaloid biosynthesis

AUTHOR(S): Faulkner, Jerome R.; Hussaini, Syed R.; Blankenship, Jimmy D.; Spiering, Martin J.; Pal, Sitaram; Grossman, Robert B.; Schardl, Christopher L.

CORPORATE SOURCE: Plant Pathology, University of Kentucky, Lexington, KY, 40546-0312, USA

SOURCE: Abstracts, 39th Central Regional Meeting of the American Chemical Society, Covington, KY, United States, May 20-23 (2007), CRM-063. American Chemical Society: Washington, D. C.  
CODEN: 69JFCV

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB *Epichloe* species and their anamorphs, *Neotyphodium* species, are fungal endophytes that inhabit cool-season grasses and often produce bioprotective alkaloids. These alkaloids include lolines, which are insecticidal and insect feeding deterrents. Lolines are

1-aminopyrrolizidines with a substituted amino group on carbon 1 and an oxygen bridge between carbons 2 and 7. In our previously published studies we showed that loline is derived from the amino acids L-proline and L-homoserine, and we also characterized the gene cluster required for loline alkaloid production. Eight synthesized deuterated compounds and deuterated proline were fed to *Neotyphodium uncinatum* in loline-producing cultures to test their possible roles as precursors or intermediates in the loline pathway. N-Formylloline was extracted from the cultures and assayed by GCMS for incorporation of the deuterium label. Using this approach we determined that N-(3-amino-3-carboxypropyl)proline and exo-1-aminopyrrolizidine are intermediates in loline alkaloid biosynthesis. A gene replacement strategy was also employed to eliminate one of the genes in the loline alkaloid cluster. The resulting fungal transformant was altered in its loline alkaloid production phenotype. The combined feeding results and gene replacement experiment were used to propose a likely sequence of bond formation in loline alkaloid biosynthesis. The first step is condensation of proline with homoserine by an unusual gamma-substitution reaction, and in the later steps an ether bridge is introduced in a chemical unusual context, after which N-methylloine is converted to N-formylloline.

L4 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2006:698366 CAPLUS

DOCUMENT NUMBER: 146:180445

TITLE: On the sequence of bond formation in loline alkaloid biosynthesis

AUTHOR(S): Faulkner, Jerome R.; Hussaini, Syed R.; Blankenship, Jimmy D.; Pal, Sitaram; Branan, Bruce M.; Grossman, Robert B.; Schardl, Christopher L.

CORPORATE SOURCE: Department of Plant Pathology, University of Kentucky, Lexington, KY, 40546-0312, USA

SOURCE: ChemBioChem (2006), 7(7), 1078-1088

CODEN: CBCHFX; ISSN: 1439-4227

Wiley-VCH Verlag GmbH

PUBLISHER:

& Co. KGaA

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 146:180445

AB Loline alkaloids are saturated pyrrolizidines with an oxygen bridge between carbon atoms C-2 and C-7 and an amino group on C-1. They are bioprotective alkaloids produced by *Epichloe* and *Neotyphodium* species, mutualistic fungal endophytes that are symbiotic with cool-season grasses. The sequence of bond formation in loline alkaloid biosynthesis was determined by synthesizing deuterated forms of potential intermediates and feeding them to cultures of the endophyte *Neotyphodium uncinatum*. These cultures incorporated deuterium from labeled N-(3-amino-3-carboxypropyl)proline and exo-1-aminopyrrolizidine into N-formylloline. The first result suggests that N-(3-amino-3-carboxypropyl)proline is the first committed intermediate in loline biosynthesis, and the second result demonstrates that the pyrrolizidine rings form before the ether bridge. The incorporation of these two compounds into loline and the lack of incorporation of several related compounds clarify the order of bond formation in loline alkaloid biosynthesis.

OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2005:540971 CAPLUS

DOCUMENT NUMBER: 143:302170

TITLE: Biosynthetic precursors of fungal pyrrolizidines, the loline alkaloids

AUTHOR(S): Blankenship, Jimmy D.; Houseknecht, Justin B.; Pal, Sitaram; Bush, Lowell P.; Grossman, Robert B.; Schardl, Christopher L.

CORPORATE SOURCE: Department of Plant Pathology, University of Kentucky, Lexington, KY, 40546-0312, USA

SOURCE: ChemBioChem (2005), 6(6), 1016-1022  
CODEN: CBCHFX; ISSN: 1439-4227

PUBLISHER: Wiley-VCH Verlag GmbH

& Co. KGaA

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Loline alkaloids are saturated pyrrolizidines with a substituted 1-amino group and an oxygen bridge between C2 and C7, and are insecticidal metabolites of plant-symbiotic fungi (endophytes). Cultures of the endophyte, *Neotyphodium uncinatum*, incorporated labeled L-proline and L-homoserine into the 1-aminopyrrolizidine, N-formylloline. The A-ring carbons C1-C3 and the N1 were derived from L-homoserine; the B-ring carbons C5-C8 and the ring nitrogen were derived from L-proline. Incorporation of both deuterium atoms from L-[4,4-2H2]homoserine and feeding tests with labeled L-methionine indicated that L-homoserine incorporation was not achieved via aspartyl semialdehyde or S-adenosylmethionine, but probably involved a highly novel N-C bond-forming  $\gamma$ -substitution reaction.

OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)

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L4 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2011 ACS ON STN

ACCESSION NUMBER: 2005:451185 CAPLUS

DOCUMENT NUMBER: 142:487686

TITLE: Antibacterial compositions comprising (alkyl)aminopyrrolizidine compounds

INVENTOR(S): Nash, Robert James; Wolferstan, Paul; Fleet, George William John; Van Ameijde, Jeroen; Horne, Graeme

PATENT ASSIGNEE(S): Molecularnature Limited, UK; M N L Pharma Limited

SOURCE: PCT Int. Appl., 24 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005046674	A2	20050526	WO 2004-GB4624	20041103
WO 2005046674	A3	20050714		
<p>W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW</p> <p>RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG</p>				

PRIORITY APPLN. INFO.: GB 2003-25655 A 20031104

OTHER SOURCE(S): MARPAT 142:487686



AB Antibacterial (alkyl)aminopyrrolizidine compds. for use in therapy or prophylaxis may be pharmaceutically acceptable derivs. of loline. Examples include 2,7-dihydroxy-1-methylaminopyrrolizidine, 2,7-dihydroxy-1-aminopyrrolizidine, 2-hydroxy-1-aminopyrrolizidine, 2-hydroxy-1-methylaminopyrrolizidine, 7-hydroxy-1-aminopyrrolizidine, 7-hydroxy-1-methylaminopyrrolizidine, 1 $\alpha$ -methylamino-2 $\beta$ -hydroxypyrrolizidine, 1 $\alpha$ -methylamino-7 $\beta$ -hydroxypyrrolizidine, 1 $\alpha$ -amino-2 $\beta$ -hydroxypyrrolizidine, 1 $\alpha$ -amino-7 $\beta$ -hydroxypyrrolizidine, 1 $\alpha$ -amino-2,7 $\beta$ -hydroxypyrrolizidine and 1 $\alpha$ -methylamino-2,7 $\beta$ -hydroxypyrrolizidine. The compds. may be used to treat infection with *Staphylococcus aureus* (MRSA), including C-MRSA1, C-MRSA2, C-MRSA3, C-MRSA4, Belgian MRSA, Swiss MRSA and any of the EMRSA strains. For example, meadow brown butterflies have activity against *Staphylococcus aureus* (MRSA) and a 50% ethanol extract of these butterflies contains the activity. Furthermore, the activity was retained by a strongly acidic cation exchange resin. The material not bound to the resin was inactive but the material displaced by 2 M ammonia solution had activity. This ammonia fraction contained various open-furan ring lolines (as determined by mass spectroscopy). Also, a semisynthetic reaction mixture derived from loline was tested for activity by incubation for 12 to 24 h at 37° at various concns. with a suspension of 1x10<sup>3</sup> c.f.u. of *Staphylococcus aureus*. After incubation, test samples were plated onto solid agar plates and colonies counted after incubation at 37° for 24 h. Complete bacterial killing was observed

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)  
 REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2005:137050 CAPLUS  
 DOCUMENT NUMBER: 142:355438  
 TITLE: A flexible carbanionic approach to protected trans-(2R,3S)-2-substituted 3-aminopyrrolidines: application to the asymmetric synthesis of (+)-absoulone  
 AUTHOR(S): Tang, Tian; Ruan, Yuan-Ping; Ye, Jian-Liang; Huang, Pei-Qiang  
 CORPORATE SOURCE: Department of Chemistry and The Key Laboratory for Chemical Biology of Fujian Province, College of Chemistry and Chemical Engineering, Xiamen University, Xiamen, 361005, Peop. Rep. China  
 SOURCE: Synlett (2005), (2), 231-234  
 CODEN: SYNLES; ISSN: 0936-5214  
 PUBLISHER: Georg Thieme Verlag  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 142:355438

AB Based on the use of Ph thioether I as a synthetic equivalent, a new carbanionic approach to trans-(2R,3S)-2-substituted 3-aminopyrrolidines, e.g. II, is described. Application of the method to the asym. synthesis of 1-aminopyrrolizidine alkaloid (+)-absoulone (III) is also reported.

OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)  
 REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2004:742196 CAPLUS

DOCUMENT NUMBER: 141:379761  
 TITLE: Reactivity of Chiral  $\alpha$ -Amidoalkyl phenyl Sulfones with Stabilized Carbanions. Stereoselective Synthesis of Optically Active 1-Aminopyrrolizidine  
 AUTHOR(S): Giri, Nicola; Petrini, Marino; Profeta, Roberto  
 CORPORATE SOURCE: Dipartimento di Scienze Chimiche, Universita di Camerino, Camerino, I-62032, Italy  
 SOURCE: Journal of Organic Chemistry (2004), 69(21), 7303-7308  
 CODEN: JOCEAH; ISSN: 0022-3263  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 141:379761

AB Metal enolates and functionalized allylzinc reagents react with optically active  $\alpha$ -amidoalkyl Ph sulfones to give N-carbamoylamino derivs. with variable levels of anti diastereoselectivity. Zinc enolates provide comparable results with respect to lithium enolates in terms of diastereoselectivity but afford  $\beta$ -amino ester derivs. in lower yield. The synthetic utility of the obtained chiral N-carbamoylamino esters is demonstrated by the first enantioselective synthesis of (-)-1-aminopyrrolizidine (I) a central intermediate for the preparation of various biol. active substances.

OS.CITING REF COUNT: 24 THERE ARE 24 CAPLUS RECORDS THAT CITE THIS RECORD (24 CITINGS)  
 REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2004:569908 CAPLUS  
 DOCUMENT NUMBER: 141:101190  
 TITLE: Cloning and sequences for gene clusters associated with biosynthesis of insecticidal loline alkaloids in the fungal endophyte Neotyphodium uncinatum, and uses in alkaloid production  
 INVENTOR(S): Schardl, Christopher L.; Wilkinson, Heather H.; Spiering, Martin J.  
 PATENT ASSIGNEE(S): University of Kentucky Research Foundation, USA  
 SOURCE: U.S. Pat. Appl. Publ., 46 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040139496	A1	20040715	US 2003-601700	20030624
US 7183098	B2	20070227		

PRIORITY APPLN. INFO.: US 2002-390446P P 20020624

AB Loline alkaloids (LA), which are 1-aminopyrrolizidines with an oxygen bridge, are produced by Epichloa (anamorph = Neotyphodium) species, endophytes of grasses. LA are insecticidal, thus helping protect host plants from insect herbivory. Suppression subtractive hybridization PCR was used to isolate transcripts up-regulated during loline alkaloid production in cultures of Neotyphodium uncinatum. Subtracted cDNAs were cloned, and a  $\lambda$ -phage cDNA library from an LA-expressing N. uncinatum culture was screened with subtracted cDNA. In BLAST searches, several cDNAs identified had sequence similarities to aspartate kinases, and another with O-acetylhomoserine-(thiol)lyase. Differential expression of these two genes in LA-producing cultures of N. uncinatum was confirmed, and in a survey of 23 isolates from 21 Neotyphodium and Epichloa species these two

genes strictly correlated with LA production Two nucleic acid mols. encoding  
two loline alkaloid gene clusters have been identified.  
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD  
(1 CITINGS)  
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2002:556216 CAPLUS  
DOCUMENT NUMBER: 138:84162  
TITLE: Expressed sequence tags and genes associated with  
loline alkaloid expression by the fungal endophyte  
Neotyphodium uncinatum  
AUTHOR(S): Spiering, Martin J.; Wilkinson, Heather H.;  
Blankenship, Jimmy D.; Schardl, Christopher L.  
CORPORATE SOURCE: Department of Plant Pathology, University of Kentucky,  
Lexington, KY, 40546-0091, USA  
SOURCE: Fungal Genetics and Biology (2002), 36(3), 242-254  
CODEN: FGBIFV; ISSN: 1087-1845  
PUBLISHER: Elsevier Science  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Lolines alkaloids (LA), which are 1-aminopyrrolizidines with an oxygen  
bridge, are produced by Epichloe (anamorph=Neotyphodium) species,  
endophytes of grasses. LA are insecticidal, thus, helping to protect host  
plants from insect herbivore. The objective of this study was to identify  
genes associated with LA biosynthesis. Suppression subtractive hybridization  
PCR was used to isolate transcripts up-regulated during LA production in  
cultures of Neotyphodium uncinatum. Subtracted cDNAs were cloned and a  
 $\lambda$ -phage cDNA library from an LA-expressing N. uncinatum culture was  
screened with subtracted cDNA. In BLAST searches, several cDNAs  
identified had sequence similarities to aspartate kinases and another with  
O-acetylhomoserine-(thiol)lyase. Differential expression of these two  
genes in LA-producing cultures of N. uncinatum was confirmed and in a  
survey of 23 isolates from 21 Neotyphodium and Epichloe species these two  
genes strictly correlated with LA production These findings open up the  
possibility for detailed studies on genes and enzymes involved in LA  
production

OS.CITING REF COUNT: 21 THERE ARE 21 CAPLUS RECORDS THAT CITE THIS  
RECORD (21 CITINGS)  
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2001:667414 CAPLUS  
DOCUMENT NUMBER: 136:2642  
TITLE: Production of loline alkaloids by the grass endophyte,  
Neotyphodium uncinatum, in defined media  
AUTHOR(S): Blankenship, J. D.; Spiering, M. J.; Wilkinson, H. H.;  
Fannin, F. F.; Bush, L. P.; Schardl, C. L.  
CORPORATE SOURCE: Department of Plant Pathology, University of Kentucky,  
Lexington, KY, 40546-0091, USA  
SOURCE: Phytochemistry (2001), 58(3), 395-401  
CODEN: PHYCAS; ISSN: 0031-9422  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Lolines (saturated 1-aminopyrrolizidines with an oxygen bridge) are  
insecticidal alkaloids produced in symbioses of certain Epichloe  
(anamorph=Neotyphodium) species (fungal endophytes) with grasses,  
particularly of the genera Lolium and Festuca. Prior to the present

study, it was unknown whether lolines were of plant or fungal origin. Neotyphodium uncinatum, the common endophyte of meadow fescue (Lolium pratense=Festuca pratensis) produced loline, N-acetylornithine, and N-formyllooline when grown in the defined minimal media at pH 5.0-7.5, with both organic and inorg. nitrogen sources and sugars as carbon sources. In contrast, lolines were not detected in complex medium cultures. GC-MS and <sup>13</sup>C NMR spectroscopic analyses confirmed the identity of the alkaloids isolated from the defined medium cultures. Lolines accumulated to ca. 700 mg/l (4 mM) in cultures with 16.7 mM sucrose and 15-30 mM asparagine, ornithine or urea. Kinetics of loline production and fungal growth were assessed in defined medium with 16.7 mM sucrose and 30 mM ornithine. The alkaloid production rate peaked after the onset of stationary phase, as is common for secondary metabolism in other microbes.

OS.CITING REF COUNT: 34 THERE ARE 34 CAPLUS RECORDS THAT CITE THIS RECORD (34 CITINGS)  
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 2000:702799 CAPLUS

DOCUMENT NUMBER: 133:360903

TITLE: Contribution of fungal loline alkaloids to protection from aphids in a grass-endophyte mutualism  
AUTHOR(S): Wilkinson, Heather H.; Siegel, Malcolm R.; Blankenship, Jimmy D.; Mallory, Allison C.; Bush, Lowell P.; Schardl, Christopher L.

CORPORATE SOURCE: Department of Plant Pathology, University of Kentucky, Lexington, 40546-0091, USA

SOURCE: Molecular Plant-Microbe Interactions (2000), 13(10), 1027-1033

CODEN: MPMLI; ISSN: 0894-0282

PUBLISHER: APS Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Fungal endophytes provide grasses with enhanced protection from herbivory, drought, and pathogens. The loline alkaloids (saturated 1-aminopyrrolizidines with an oxygen bridge) are fungal metabolites often present in grasses with fungal endophytes of the genera Epichloe or Neotyphodium. Mendelian genetic anal. was conducted to test for activity of lolines produced in plants against aphids feeding on those plants. Though most loline-producing endophytes are asexual, it was found that a recently described sexual endophyte, Epichloe festucae, had heritable variation for loline alkaloid expression (Lol+) or nonexpression (Lol-). By analyzing segregation of these phenotypes and of linked DNA polymorphisms in crosses, we identified a single genetic locus controlling loline alkaloid expression in those E. festucae parents. We then tested segregating Lol+ and Lol- full-sibling fungal progeny for their ability to protect host plants from two aphid species, and observed that alkaloid expression cosegregated with activity against these insects. The in planta loline alkaloid levels correlated with levels of anti-aphid activity. These results suggested a key role of the loline alkaloids in protection of host plants from certain aphids, and represent, to our knowledge, the first Mendelian anal. demonstrating how a fungal factor contributes protection to plant-fungus mutualism.

OS.CITING REF COUNT: 50 THERE ARE 50 CAPLUS RECORDS THAT CITE THIS RECORD (51 CITINGS)  
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 1999:512191 CAPLUS

DOCUMENT NUMBER: 131:297587  
TITLE: Phytochemistry and chemotaxonomy of the convolvulaceae. Part 8. Occurrence of loline alkaloids in *Argyrea mollis* (Convolvulaceae)  
AUTHOR(S): Tofern, Britta; Kaloga, Macki; Witte, Ludger; Hartmann, Thomas; Eich, Eckart  
CORPORATE SOURCE: Institut für Pharmazie II (Pharmazeutische Biologie), Freie Universität Berlin, Berlin, D-14195, Germany  
SOURCE: Phytochemistry (1999), 51(8), 1177-1180  
CODEN: PYTCAS; ISSN: 0031-9422  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB N-Formylloline was isolated from roots of *Argyrea mollis*. This is the first identification of a 1-aminopyrrolizidine alkaloid (loline alkaloid) in a species of the Convolvulaceae. Loline is only known from the genus *Adenocarpus* (Fabaceae) and certain grasses (e.g. *Festuca*) infected with endophytic fungi. A GC-MS anal. revealed N-formylloline to be present in roots and aerial vegetative plant parts. It is accompanied by three congeners (i.e. loline, N-methyloline and N-propionylnorloline) and simple pyrrolidine alkaloids such as hygrine and its derivs. as well as tropan-3 $\beta$ -ol. Loline could not be detected in *Argyrea capitata*, *A. hookeri*, *A. nervosa* and numerous species of 14 other convolvulaceae genera.

OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)  
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 1997:13947 CAPLUS  
DOCUMENT NUMBER: 126:129331  
ORIGINAL REFERENCE NO.: 126:24941a, 24944a  
TITLE: Levels and tissue distribution of loline alkaloids in endophyte-infected *Festuca pratensis*  
AUTHOR(S): Justus, Mathias; Witte, Ludger; Hartmann, Thomas  
CORPORATE SOURCE: Inst. Pharmazeutische Biol., Technischen Univ. Braunschweig, Braunschweig, D-38106, Germany  
SOURCE: Phytochemistry (1996), Volume Date 1997, 44(1), 51-57  
CODEN: PYTCAS; ISSN: 0031-9422  
PUBLISHER: Elsevier  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB *Festuca pratensis* (meadow fescue) infected with the endophyte *Acremonium uncinatum* produces loline alkaloids (1-aminopyrrolizidines) that are not found in the uninfected grass or the fungus alone. Five alkaloids were identified by capillary GC and GC-MS: N-formylloline as the major compound, followed by N-acetyloline, N-acetylnorloline and trace amts. of loline and N-methyloline. A routine procedure for the extraction and sensitive quant. anal. of loline alkaloids by capillary GC is described. The loline alkaloid levels and concns. were followed quant. over the growing season of the grass-endophyte association. A detailed anal. of the tissue distribution of the alkaloids is given. The total alkaloid level per plant increases from almost zero in early spring and reaches its highest level during seed maturation. It drops to almost zero with seed dispersal and stalk senescence but increases again during the subsequent period of vegetative growth in late summer. The highest alkaloid concns. were found in young leaves in early spring, and in panicles (spikelets, seeds) and leaf pseudostems during the period of vegetative growth in late summer and autumn. During seed germination loline alkaloids are not degraded, however, a significant proportion (about 20%) are lost by leaching, mainly

during seed imbibition. Within a seed the embryo was found to contain a two-fold higher alkaloid concentration than the remaining seed tissue.

OS.CITING REF COUNT: 22 THERE ARE 22 CAPLUS RECORDS THAT CITE THIS RECORD (22 CITINGS)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 1996:557215 CAPLUS

TITLE: Epichloe species: fungal symbionts of grasses

AUTHOR(S): Schardl, Christopher L.

CORPORATE SOURCE: Department of Plant Pathology, University of Kentucky, Lexington, KY, 40546-0091, USA

SOURCE: Annual Review of Phytopathology (1996), 34, 109-130

CODEN: APPYAG; ISSN: 0066-4286

PUBLISHER: Annual Reviews

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Epichloe species and their asexual descendants (Acremonium endophytes) are fungal symbionts of C3 grasses that span the symbiotic continuum from antagonism to mutualism depending on the relative importance, resp., of horizontal transmission of sexual spores vs. vertical clonal transmission in healthy grass seeds. At least seven sexual Epichloe species are identifiable by mating tests, and many asexual genotypes are interspecific hybrids. Benefits conferred by the symbionts on host plants include protection from biotic factors and abiotic stresses such as drought. Four classes of beneficial alkaloids are associated with the symbionts: ergot alkaloids, indole diterpenes (lolitremes), peramine, and saturated aminopyrrolizidines (lolines). These alkaloids protect host plants from insect and vertebrate herbivores, including livestock. Genetic engineering of the fungal symbionts as more suitable biol. protectants for forage grasses requires identification of fungal genes for alkaloid biosynthesis, and DNA-mediated transformation of the fungi.

OS.CITING REF COUNT: 48 THERE ARE 48 CAPLUS RECORDS THAT CITE THIS RECORD (48 CITINGS)

L4 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 1988:52767 CAPLUS

DOCUMENT NUMBER: 108:52767

ORIGINAL REFERENCE NO.: 108:8753a,8756a

TITLE: Plants of New Caledonia. Part 109. Absoulone, a new pyrrolizidine alkaloid from Hugonia oreogena and Hugonia penicillanthemum

AUTHOR(S): Ikhiri, Khalid; Ahond, A.; Poupat, C.; Potier, P.; Pusset, J.; Sevenet, T.

CORPORATE SOURCE: Fac. Sci., Univ. Niamey, Niamey, 10662, Niger

SOURCE: Journal of Natural Products (1987), 50(4), 626-30

CODEN: JNPRDF; ISSN: 0163-3864

DOCUMENT TYPE: Journal

LANGUAGE: French

AB Absoulone (I), and 3 derived 1-aminopyrrolizidine-type alkaloids, were isolated from H. oreogena and H. penicillanthemum. Traces of 5-methoxy-N,N-dimethyltryptamine were also found. Structures were determined by usual spectroscopic methods.

OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)

L4 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2011 ACS on STN

ACCESSION NUMBER: 1978:406461 CAPLUS

DOCUMENT NUMBER: 89:6461

ORIGINAL REFERENCE NO.: 89:1111a,1114a

TITLE: Genus Crotalaria: part XXXI. Preparation of pharmacodynamic compounds based on 1-methylenepyrrolizidine

AUTHOR(S): Suri, K. A.; Suri, O. P.; Sawhney, R. S.; Gupta, O. P.; Atal, C. K.

CORPORATE SOURCE: Reg. Res. Lab., Jammu-Tawi, India

SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1977), 15B(10), 972-3  
CODEN: IJSBDB; ISSN: 0376-4699

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The methylenepyrrolizidine I (Z = CH<sub>2</sub>) underwent ozonolysis to give I (Z = O), the picrate of which underwent successive oximation, neutralization by ion exchange chromatog., and the reduction to give a cis-trans mixture of I (Z = H<sub>2</sub>N, H) (II). Condensation of II with BzOH in the presence of dicyclohexylcarbodiimide gave I (Z = BzNH, H). I (Z = HON) possessed cardiotonic activity in the guinea pig at 500 µg-2 mg. The quaternary ammonium salts from reaction of 4-PhC<sub>6</sub>H<sub>4</sub>COCH<sub>2</sub>Br with heliotridane and I (Z = CH<sub>2</sub>) possessed spasmolytic activity comparable to that of papaverine.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

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(FILE 'HOME' ENTERED AT 19:33:14 ON 04 AUG 2011)

FILE 'CAPLUS' ENTERED AT 19:33:19 ON 04 AUG 2011

L1 140 S LOLINE

L2 1 S L1 AND BACTERIA

L3 2 S L1 AND (ANTIINFECTIVE OR ANTIBACTERIAL)

L4 17 S AMINOPYRROLIZIDINE

=>